

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method for predicting one or more locations of single nucleotide polymorphisms in a nucleic acid sequence, comprising the steps of:

calculating a variation frequency from a first base to a second base within a group of bases in a dataset of two or more genes;

generating a variation predictiveness matrix from the calculated variation frequency;

comparing the nucleic acid sequence one or more groups at a time with the variation predictiveness matrix to assign a variation value to the bases in the nucleic acid sequence; and

identifying the locations of a variation in one or more bases of the nucleic acid sequence where single nucleotide polymorphisms will likely occur based on the assigned variation value.

Claim 2 (previously presented): The method of claim 1, further comprising one or more nucleic acid sequences with chemical modifications.

Claim 3 (previously presented): The method of claim 2, wherein the chemical modifications include methylation or other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid bases or to the nucleic acid sequence as a whole.

Claim 4 (cancelled)

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 5 (previously presented): The method of claim 1, wherein the variation in one or more bases is nonsynonymous.

Claim 6 (previously presented): The method of claim 1, wherein the variation in one or more bases is synonymous.

Claim 7 (original): The method of claim 1, further comprising the step of generating a dataset of single nucleotide polymorphisms for one or more nucleic acid sequences.

Claim 8 (cancelled)

Claim 9 (previously presented): The method of claim 1, wherein the dataset comprises genes with nucleic acid chemical modifications.

Claim 10 (original): The method of claim 9, wherein the chemical modifications include methylation or other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid bases or to the nucleic acid sequence as a whole.

Claim 11 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a known mutation dataset.

Claim 12 (previously presented): The method of claim 1, wherein the variation frequency is determined from a dataset of known diseases.

Claim 13 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a dbSNP database.

Claim 14 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a non-human mutation database.

Claim 15 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a disease-specific database.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 16 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a non-human disease database.

Claim 17 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a HGMD database.

Claim 18 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a linkage database.

Claim 19 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a splice variant database.

Claim 20 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a translocation database.

Claim 21 (withdrawn): The method of claim 8, wherein the variation frequency is determined from a database of known mutations.

Claim 22 (previously presented): The method of claim 1, wherein the variation frequency is adjusted for wild type genes.

Claim 23 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for engineered or non-naturally occurring genes.

Claim 24 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for conservative polymorphisms.

Claim 25 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for non-conservative polymorphisms.

Claim 26 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for cDNA stability.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 27 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for predicted DNA structure.

Claim 28 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for predicted RNA structure.

Claim 29 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for predicted protein structure.

Claim 30 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for post-translational modification sequences.

Claim 31 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for protein stability.

Claim 32 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for predicted protein transport.

Claim 33 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for shuffled genes.

Claim 34 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for site-directed mutagenesis genes.

Claim 35 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for methylated sequences

Claim 36 (withdrawn): The method of claim 8, wherein the variation frequency is further adjusted for epigenetic variation.

Claim 37 (previously presented): The method of claim 1, wherein the nucleic acid sequence comprises a cDNA sequence.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 38 (previously presented): The method of claim 1, wherein the nucleic acid sequence comprises a genomic sequence.

Claim 39 (previously presented): The method of claim 1, wherein the nucleic acid sequence comprises an intron/exon boundary.

Claim 40 (previously presented): The method of claim 1, wherein the nucleic acid sequence comprises a transcriptional control sequence.

Claim 41 (previously presented): The method of claim 1, wherein the nucleic acid sequence comprises a transport control sequence.

Claim 42 (previously presented): The method of claim 1, wherein the nucleic acid sequence comprises a translational control sequence.

Claim 43 (cancelled)

Claim 44 (previously presented): The method of claim 1, wherein the nucleic acid sequence comprises a splicing control sequence.

Claim 45 (previously presented): The method of claim 1, wherein the variation predictiveness matrix correlates a frequency of a first codon mutation to a second codon mutation with a variation predictiveness value of the nucleic acid sequence from one to ten bases at a time.

Claim 46 (original): The method of claim 1, wherein the variation predictiveness matrix is normalized for the codon usage of a target organism.

Claim 47 (original): The method of claim 1, wherein the variation predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 48 (original): The method of claim 1, wherein the variation predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database minus the known mutant genes of the mutant gene dataset.

Claim 49 (original): The method of claim 1, wherein the nucleic acid sequence comprises an entire genome.

Claim 50 (original): The method of claim 1, wherein the nucleic acid sequence comprises a human genome.

Claim 51 (original): The method of claim 1, wherein the nucleic acid sequence comprises a gene cluster for a target human disease.

Claim 52 (original): The method of claim 1, wherein the variation predictiveness matrix is based on a mutant gene dataset that comprises a human mutation database.

Claim 53 (previously amended): The method of claim 1, wherein the steps are effected by a computer program.

Claim 54 (cancelled)

Claim 55 (cancelled)

Claim 56 (original): The method of claim 1, wherein the variation predictiveness matrix is determined in silico from a human mutant database.

Claim 57 (currently amended): The method of claim 1, wherein the step of comparing the nucleic acid sequence ~~three or more bases~~ one or more groups at a time with the variation predictiveness matrix to assign a variation value to the bases in the nucleic acid sequence is determined in silico.

Claim 58 (withdrawn): A method for creating a variation predictiveness value for use in a variation predictiveness matrix, comprising the steps of:

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

calculating the variation frequency from a first nucleic acid to a second nucleic acid in a dataset of two or more variations; and

determining a variation predictiveness value from the calculated variation frequency.

Claim 59 (withdrawn): The method of claim 58, further comprising the step of generating a variation predictiveness matrix that correlates the frequency of a first to a second variation with the variation predictiveness value.

Claim 60 (withdrawn): The method of claim 58, wherein the dataset comprises genes with nucleic acid chemical modifications.

Claim 61 (withdrawn): The method of claim 60, wherein the chemical modifications includemethylation or other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid bases or to the nucleic acid as a whole.

Claim 62 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a known mutation dataset.

Claim 63 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a dataset of known diseases.

Claim 64 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a dbSNP database.

Claim 65 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a non-human mutation database.

Claim 66 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a disease-specific database.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 67 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a non-human disease database.

Claim 68 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a HGMD database.

Claim 69 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a linkage database.

Claim 70 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a splice variant database.

Claim 71 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a translocation database.

Claim 72 (withdrawn): The method of claim 58, wherein the variation frequency is determined from a database of known mutations.

Claim 73 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for wild type genes.

Claim 74 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for engineered or non-naturally occurring genes.

Claim 75 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for conservative polymorphisms.

Claim 76 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for non-conservative polymorphisms.

Claim 77 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for cDNA stability.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 78 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for predicted DNA structure.

Claim 79 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for predicted RNA structure.

Claim 80 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for predicted protein structure.

Claim 81 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for post-translational modification sequences.

Claim 82 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for protein stability.

Claim 83 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for predicted protein transport.

Claim 84 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for shuffled genes.

Claim 85 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for site-directed mutagenesis genes.

Claim 86 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for methylated sequences

Claim 87 (withdrawn): The method of claim 58, wherein the variation frequency is further adjusted for epigenetic variation.

Claim 88 (withdrawn): The method of claim 58, wherein the variations comprise a cDNA sequence.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 89 (withdrawn): The method of claim 58, wherein the variations comprise genomic sequence.

Claim 90 (withdrawn): The method of claim 58, wherein variations comprise an intron/exon boundary.

Claim 91 (withdrawn): The method of claim 58, wherein variations comprise exons.

Claim 92 (withdrawn): The method of claim 58, wherein variations comprise other SNPs.

Claim 93 (withdrawn): The method of claim 58, wherein variations comprise inversions.

Claim 94 (withdrawn): The method of claim 58, wherein variations comprise deletions.

Claim 95 (withdrawn): The method of claim 58, wherein variations comprise splice variations.

Claim 96 (withdrawn): The method of claim 58, wherein variations comprise translocations.

Claim 97 (withdrawn): The method of claim 58, wherein variations comprise a transcriptional control sequence.

Claim 98 (withdrawn): The method of claim 58, wherein variations comprise a transport control sequence.

Claim 99 (withdrawn): The method of claim 58, wherein variations comprise a translational control sequence.

Claim 100 (withdrawn): The method of claim 58, wherein variations comprise a transcriptional control sequence.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 101 (withdrawn): The method of claim 58, wherein variations comprise a splicing control sequence.

Claim 102 (withdrawn): The method of claim 59, wherein in the variation predictiveness matrix is normalized for the nucleotide usage of a target organism.

Claim 103 (withdrawn): The method of claim 59, wherein the variation predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database.

Claim 104 (withdrawn): The method of claim 58, wherein the variation predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database minus the known mutant genes of the mutant gene dataset.

Claim 105 (withdrawn): The method of claim 58, where the nucleic acid comprises one or more bases.

Claim 106 (withdrawn): The method of claim 58, where the nucleic acid comprises DNA.

Claim 107 (withdrawn): The method of claim 58, where the nucleic acid comprises RNA.

Claim 108 (withdrawn): The method of claim 58, where the nucleic acid comprises a triplet.

Claim 109 (withdrawn): The method of claim 58, The method of claim 16, where the nucleic acid comprises a codon.

Claim 110 (withdrawn): The method of claim 58, The method of claim 16, where the nucleic acid comprises one or more non-sequence base modifications.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 111 (withdrawn): The method of claim 58, where the nucleic acid comprises modified nucleic acids.

Claim 112 (withdrawn): The method of claim 58, wherein modified nucleic acids include methylation or other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid bases or to the nucleic acid as a whole.

Claim 113 (withdrawn): The method of claim 58, where the nucleic acid comprises an entire genome.

Claim 114 (withdrawn): The method of claim 58, where the nucleic acid comprises a human genome.

Claim 115 (withdrawn): The method of claim 58, where the nucleic acid comprises a gene cluster for a target human disease.

Claim 116 (withdrawn): The method of claim 58, where the variation predictiveness matrix is based on a mutant gene dataset that comprises a human mutation database.

Claim 117 (withdrawn): The method of claim 58, wherein the steps are affected by a computer program.

Claim 118 (withdrawn): The method of claim 58, wherein the computer program is SNIDE.

Claim 119 (withdrawn): The method of claim 58, wherein the computer program is SNooP.

Claim 120 (withdrawn): The method of claim 58, wherein the variation predictiveness value is determined in silico from a human mutant database.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 121 (withdrawn): The method of claim 58, wherein the step of predicting a likelihood of one or more single nucleotide variation is determined in silico.

Claim 122 (withdrawn): A method for creating a polymorphism predictiveness value for use in a mutation predictiveness matrix, comprising the steps of:

calculating the mutation frequency from a first codon to a second codon in a dataset of two or more mutant genes; and

determining a polymorphism predictiveness value from the calculated mutation frequency.

Claim 123 (withdrawn): The method of claim 122, further comprising the step of generating a codon polymorphism predictiveness matrix that correlates the frequency of a first to a second codon mutation with the polymorphism predictiveness value.

Claim 124 (withdrawn): The method of claim 122, wherein the dataset comprises nucleic acids with chemical modifications.

Claim 125 (withdrawn): The method of claim 124, wherein the chemical modifications include methylation or other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid bases or to the nucleic acid as a whole.

Claim 126 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a known mutation dataset.

Claim 127 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a dataset of known diseases.

Claim 128 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a dbSNP database.

Claim 129 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a non-human mutation database.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 130 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a disease-specific database.

Claim 131 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a non-human disease database.

Claim 132 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a HGMD database.

Claim 133 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a linkage database.

Claim 134 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a splice variant database.

Claim 135 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a translocation database.

Claim 136 (withdrawn): The method of claim 122, wherein the mutation frequency is determined from a database of known mutations.

Claim 137 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for wild type genes.

Claim 138 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for engineered or non-naturally occurring genes.

Claim 139 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for conservative polymorphisms.

Claim 140 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for non-conservative polymorphisms.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 141 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for cDNA stability.

Claim 142 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for predicted DNA structure.

Claim 143 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for predicted RNA structure.

Claim 144 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for predicted protein structure.

Claim 145 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for post-translational modification sequences.

Claim 146 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for protein stability.

Claim 147 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for predicted protein transport.

Claim 148 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for shuffled genes.

Claim 149 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for site-directed mutagenesis genes.

Claim 150 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for methylated sequences

Claim 151 (withdrawn): The method of claim 122, wherein the mutation frequency is further adjusted for epigenetic variation.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 152 (withdrawn): The method of claim 122, wherein the mutant genes comprise a cDNA sequence.

Claim 153 (withdrawn): The method of claim 122, wherein the mutant genes comprise genomic sequence.

Claim 154 (withdrawn): The method of claim 122, wherein mutant genes comprise an intron/exon boundary.

Claim 155 (withdrawn): The method of claim 122, wherein mutant genes comprise exons.

Claim 156 (withdrawn): The method of claim 122, wherein mutant genes comprise other SNPs.

Claim 157 (withdrawn): The method of claim 122, wherein mutant genes comprise inversions.

Claim 158 (withdrawn): The method of claim 122, wherein mutant genes comprise deletions.

Claim 159 (withdrawn): The method of claim 122, wherein mutant genes comprise splice variations.

Claim 160 (withdrawn): The method of claim 122, wherein mutant genes comprise translocations.

Claim 161 (withdrawn): The method of claim 122, wherein mutant genes comprise a transcriptional control sequence.

Claim 162 (withdrawn): The method of claim 122, wherein mutant genes comprise a transport control sequence.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 163 (withdrawn): The method of claim 122, wherein mutant genes comprise a translational control sequence.

Claim 164 (withdrawn): The method of claim 122, wherein mutant genes comprise a transcriptional control sequence.

Claim 165 (withdrawn): The method of claim 122, wherein mutant genes comprise a splicing control sequence.

Claim 166 (withdrawn): The method of claim 123, wherein in the codon polymorphism predictiveness matrix is normalized for the codon usage of a target organism.

Claim 167 (withdrawn): The method of claim 123, wherein the codon polymorphism predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database.

Claim 168 (withdrawn): The method of claim 123, wherein the codon polymorphism predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database minus the known mutant genes of the mutant gene dataset.

Claim 169 (withdrawn): The method of claim 122, where the codon comprises one or more bases.

Claim 170 (withdrawn): The method of claim 122, where the codon comprises DNA.

Claim 171 (withdrawn): The method of claim 122, where the codon comprises RNA.

Claim 172 (withdrawn): The method of claim 122, where the codon comprises a triplet.

Claim 173 (withdrawn): The method of claim 122, where the codon comprises a codon.

Claim 174 (withdrawn): The method of claim 122, where the codon comprises one or more non- sequence base modifications.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 175 (withdrawn): The method of claim 122, wherein the codon further comprises modifications.

Claim 176 (withdrawn): The method of claim 122, wherein modifications include methylation or other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid bases or to the nucleic acid as a whole.

Claim 177 (withdrawn): The method of claim 122, where the codon comprises an entire genome.

Claim 178 (withdrawn): The method of claim 122, where the codon comprises a human genome.

Claim 179 (withdrawn): The method of claim 122, where the codon comprises a gene cluster for a target human disease.

Claim 180 (withdrawn): The method of claim 122, where the codon polymorphism predictiveness matrix is based on a mutant gene dataset that comprises a human mutation database.

Claim 181 (withdrawn): The method of claim 122, wherein the step of predicting a likelihood of one or more single nucleotide polymorphisms is determined in silico.

Claim 182 (withdrawn): A method for creating a variation predictiveness matrix, comprising the steps of:

- calculating the variation frequency from a first nucleic acid to a second nucleic acid in a dataset of two or more variations;

- determining a variation predictiveness value from the calculated variation frequency; and

- generating a variation predictiveness matrix that correlates the frequency of a first to a second nucleic acid with the variation predictiveness value.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 183 (withdrawn): The method of claim 182, wherein the dataset comprises nucleic acids with chemical modifications.

Claim 184 (withdrawn): The method of claim 183, wherein the chemical modifications include methylation or other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid bases or to the nucleic acid as a whole.

Claim 185 (withdrawn): The method of claim 182, wherein the variation frequency is determined from a variation dataset.

Claim 186 (withdrawn): A method for creating a polymorphism predictiveness matrix, comprising the steps of:

- calculating the mutation frequency from a first codon to a second codon in a dataset of two or more mutant genes;

- determining a polymorphism predictiveness value from the calculated mutation frequency; and

- generating a codon polymorphism predictiveness matrix that correlates the frequency of a first to a second codon mutation with the polymorphism predictiveness value.

Claim 187 (withdrawn): The method of claim 186, wherein the dataset comprises nucleic acids with chemical modifications.

Claim 188 (withdrawn): The method of claim 187, wherein the chemical modifications include methylation or other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid bases or to the nucleic acid as a whole.

Claim 189 (withdrawn): The method of claim 186, wherein in the codon polymorphism predictiveness matrix is normalized for the codon usage of a target organism.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 190 (withdrawn): The method of claim 186, wherein the codon polymorphism predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database.

Claim 191 (withdrawn): The method of claim 186, wherein the codon polymorphism predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database minus the known mutant genes of the mutant gene dataset.

Claim 192 (withdrawn): The method of claim 186, wherein the codon comprises one or more bases.

Claim 193 (withdrawn): The method of claim 186, where the codon comprises a triplet.

Claim 194 (withdrawn): The method of claim 186, where the codon comprises a codon.

Claim 195 (withdrawn): The method of claim 186, where the codon comprises one or more non-sequence base modifications.

Claim 196 (withdrawn): An isolated and purified nucleic acid comprising a predicted single nucleotide variation of a nucleic acid sequence based on the variation predictiveness matrix sequence of claim 1.

Claim 197 (withdrawn): An isolated and purified nucleic acid comprising a predicted single nucleotide polymorphism of a wild-type gene sequence based on the codon mutation predictiveness matrix sequence of claim 1.

Claim 198 (withdrawn): An apparatus for detecting a single nucleotide polymorphism comprising:

a substrate; and

one or more isolated and purified nucleic acids comprising a predicted single nucleotide variation of a nucleic acid sequence based on a variation predictiveness matrix sequence affixed to the substrate.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 199 (withdrawn): The apparatus of claim 198, wherein the substrate comprises a microfabricated solid surface to which molecules may be attached through either covalent or non-covalent bonds.

Claim 200 (withdrawn): The apparatus of claim 198, wherein the substrate further comprises Langmuir-Bodgett films, glass, functionalized glass, germanium, silicon, PTFE, polystyrene, gallium arsenide, gold, silver, or any materials comprising amino, carboxyl, thiol or hydroxyl functional groups incorporated on a planar or spherical surface.

Claim 201 (withdrawn): An apparatus for detecting a single nucleotide polymorphism comprising:

a substrate; and

one or more isolated and purified nucleic acids comprising a predicted single nucleotide polymorphism of a wild-type gene sequence based on a codon polymorphism predictiveness matrix. sequence affixed to the substrate.

Claim 202 (withdrawn): The apparatus of claim 201, wherein the substrate comprises a microfabricated solid surface to which molecules may be attached through either covalent or non-covalent bonds.

Claim 203 (currently amended): A computer program embodied on a computer readable medium for predicting one or more locations of variations in a wild-type gene sequence, comprising:

a code segment for calculating a variation frequency from a first base to a second base within a group of bases in a nucleic acid dataset;

a code segment for generating a variation predictiveness matrix from the calculated variation frequency;

a code segment for comparing the wild-type gene sequence one or more groups at a time with the variation predictiveness matrix to assign a variation value to the bases in the wild-type gene sequence; and

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

a code segment for identifying one or more locations ~~that will likely cause where~~ a variation is likely to occur in one or more bases of the wild-type gene sequence based on the assigned variation value.

Claim 204 (currently amended): A computer program embodied on a computer readable medium for predicting one or more locations of polymorphisms in a wild-type gene sequence, comprising:

a code segment for calculating a variation frequency from a first codon to a second codon in a mutant gene dataset;

a code segment for generating a codon mutation predictiveness matrix from the calculated variation frequency;

a code segment for comparing the wild-type gene sequence one or more codons at a time with the codon mutation predictiveness matrix to assign a variation value to the codons in the wild-type gene sequence; and

a code segment for identifying one or more locations ~~that will likely cause where~~ a variation is likely to occur in one or more codons in the wild-type gene sequence based on the assigned variation value.

Claim 205 (withdrawn): A polymorphism prediction dataset, comprising:

a first nucleic acid;

a second nucleic acid variation that correlates to a polymorphism from the first nucleic acid; and

a variation predictiveness value determined from known variations in a variation database for a target organism.

Claim 206 (withdrawn): A polymorphism prediction dataset, comprising:

a first codon;

a second codon mutation that correlates to a mutation from the first codon; and

a codon polymorphism predictiveness value determined from known mutations in a mutation database for a target organism.

Appl. No. 09/998,904
Amdt. dated Oct. 10, 2006
Reply to Office Action of Apr. 10, 2006

Claim 207 (withdrawn): A single nucleotide polymorphism determined by the method of claim 1.

Claim 208 (withdrawn): A method for predicting single nucleotide polymorphisms, comprising the steps of:

- inputting each codon in a queried nucleic acid sequence;
- determining each possible nonsynonymous mutation;
- assigning a predictiveness value to that mutation based on the identity of the wild-type and resultant codon; and
- ranking of all predictiveness values to highlight the likely to occur and impact gene function.

Claim 209 (withdrawn): The method of claim 208, further comprising the steps of:

- parsing one or more nucleic acid sequence input files having sequence information;
- calculating an expected mutation likelihood according to a user-defined threshold;
- and
- ranking of point mutation predictions by a ζ -value.

Claim 210 (withdrawn): The method of claim 208, further comprising the step of generating a delimited file suitable for a standard spreadsheet application.

Claim 211 (withdrawn): An isolated and purified nucleic acid comprising SEQ ID NOS.: 1-12.

Claim 212 (withdrawn): An isolated and purified nucleic acid comprising a cardiomyopathy disease related SNP selected from the group consisting essentially of BDKRB2, EDNRA, ADRB1, ADRB2, CREB1 and MCIP.

Claim 213 (withdrawn): An isolated and purified nucleic acid of claim 211, wherein the SNP is Thr->Met substitution in BDKRB2 at position 383.